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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,695	06/08/2001	John R. Desjarlais	16380-002001	8902
26161	7590	12/15/2006		
FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER MORAN, MARJORIE A	
			ART UNIT	PAPER NUMBER
			1631	
DATE MAILED: 12/15/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/877,695

Applicant(s)

DESJARLAIS, JOHN R.

Examiner

Marjorie A. Moran

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-7, 14-18, 38-50, 60, 61, 67 and 68 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 3, 5-7, 14-17, 44, 61 and 67 is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4, 18, 38-43, 45-50, 60 and 68 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |  |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. <u>9/12/06</u>                              |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application  |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                           |

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 38, 47, 60, and 68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

A method of generating a probability matrix comprising generating an output of the probability matrix, as recited in amended claim 1, is new matter. The original claims and drawings did not recite or show any output steps. The originally filed specification, on page 27, lines 25-27 discloses that Fig. 5 is a display of a portion of a "free energy matrix," thus providing support for display of a free energy matrix. However, page 27 also defines a free energy matrix to be one "representing the lowest free energy rotamer state of each amino acid type at all positions." The probability matrix of claim 1 is not limited to comprise or represent the LOWEST free energy ROTAMER STATE of each amino acid type, but merely represents "energy fitness" of amino acids at each position of a variant protein sequence. Claim 1 does not recite any limitation with regard to rotamer states of amino acids. As the probability matrix of claim 1 appears to be different from the free energy matrix displayed in Figure 5, neither page 27 nor Figure 5

provide support for “generating an output” of a probability matrix, as newly recited in claim 1.

A method comprising generating “at least one protein sequence” from a probability matrix and comprising generating an output of “at least one protein sequence” as recited in amended claims 2, 38 and 68, is also new matter. A method of producing “at least one protein” as recited in claim 60 (introduce by amendment on 11/17/03) is also new matter. Original claims 2, 10, and 25 recited “generating a single protein sequence” from a probability matrix and original claims 3, 11, and 26 recited generating a combinatorial library of proteins from the matrix. The original claims did not recite *producing* an actual protein anywhere. Nowhere did the original claims recite generating or producing multiple protein sequences which were not members of a combinatorial library. The originally filed specification discloses on page 19 and page 20, line 30- page 21, line 3 (example 1) that a free energy matrix may be used to design a “single optimal protein” which may then be physically produced, thus providing support for both generating a producing a SINGLE protein. The specification also discloses on page 19, lines 22-28 and in Example 2 that a probability matrix or free energy matrix may be used to design combinatorial libraries of proteins. Nowhere does the originally filed specification disclose designing or producing multiple proteins which are not members of a combinatorial library. Thus, methods comprising generating or producing “at least one protein sequence” from a probability matrix are new matter. The original claims did not recite any step of outputting. The originally filed specification on pages 30-31 discloses that Figure 8 displays a variety of combinatorial libraries of

proteins generated from a probability matrix. However, neither the originally filed specification or drawings provide support for display of a single protein generated from a probability matrix, not for display of a plurality or proteins which are not members of a combinatorial library. Thus, a step of generating an "output" of "at least one protein sequence" is also new matter.

Applicant argues in the response filed 9/29/06 that the I/O devices of Figure 1 provide support for "providing an output." In response, it is noted that while an I/O device is capable of providing an output, that does not mean that the device actually performs in this manner. Further, one skilled in the art would not have recognized that applicant contemplated specific steps of outputting particular information or data as part of the inventive method at the time of filing merely because an I/O device is shown in a block diagram of a device. The specification discloses many examples of inputting information (e.g. backbone structure ensembles), but none for outputting, thus it is clear that the I/O device was intended to be used for inputting information for use in the method, but it is not clear that the device was intended to be used to output anything. Applicant does not point to support anywhere for the newly recited step of generating "at least one protein sequence" recited in amended claim 2. For these reasons, the arguments are not persuasive, and the claims are rejected for reciting new matter.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 18, 38-43,45, 46, 48-50, and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 limits the method of 3 to one wherein steps are repeated more than once, but does not identify which steps are to be repeated. As it is unclear whether all the steps or some subset; i.e. only those required "to generate the probability matrix" are to be repeated, claim 4 is indefinite.

Claims 18, 38, 42, 45, and 46 recite apparent method steps in passive voice. It is unclear whether applicant intends to limit a parent claim to further include another step (e.g. combining information, selecting a protein sequence, combining probability matrices, iterating a process, and/or expressing functions or a value), or is some limitation of data is intended. If the former, then the claims should clearly recite further steps using active, positive verbs. If the latter, then it is further unclear what limitation of a method is intended by limiting data.

Claim 39 recites a step of "generating the combinatorial library." However, parent claim 3 recites a step of generating a combinatorial library, as well. It is unclear whether the step of claim 39 is intended to replace the step of claim 3, is intended to complement the step of claim 3, is an additional step of generating the library (i.e. the library is generated more than once) or if some other limitation is intended. As the limitation intended by a repetitive step of generation is unclear, claim 39 is indefinite.

Claim 40 recites a step of incorporating amino acids, but does not recite into what the amino acids are to be incorporated or at which step they are to be

incorporated. As the time and place intended for the incorporation are unclear, the claim is indefinite.

Claim 40 recites a step of “generating a library of protein sequences” in line 3. Parent claim 3 recites a step of generating a combinatorial library, this it is unclear whether the generation step of claim 40 is intended to replace the generation step of claim 3, is an adjunct to the step of claim 3, or whether some other limitation is intended with regard to “generating.” Further, it is unclear whether the “library of protein sequences” of claim 40 is intended to be different than the “combinatorial library” generated in claim 3.

Claim 43 recites “the combining process” in lines 1-2, which phrase lacks antecedent basis in the claims. Parent claim 18 does not recite a “combining process.”

Claim 48 recites a further step of screening or selecting proteins from a library. It is unclear where/when in the method of claim 61 the screening or selecting step is intended to occur, therefore claim 48 is indefinite.

Claim 48 recites “the library” in line 2. It is unclear whether the antecedent basis for this phrase is intended to be the “combinatorial library” generated in claim 61 or a different library, therefore claim 48 is indefinite.

Claim 50 depends from claim 48 and is therefore also indefinite for these reasons.

Claim 68 recites producing a protein (single) comprising “at least one protein sequence.” It is unclear whether applicant intends the produced protein to comprise a single sequence or multiple sequences (e.g. a fusion protein?), therefore claim 68 is

indefinite. It is noted that the originally filed disclosure does not provide support for producing a protein comprising multiple sequences; however, as it is unclear what is intended, the claim is rejected herein only for indefiniteness.

### ***Allowable Subject Matter***

The following is an examiner's statement of reasons for allowance: the prior art does not teach or fairly suggest the methods claimed, as argued by applicant in previous responses. Claim 3 recites a concrete, tangible and useful result, as argued by applicants, and is statutory. Claims 5-7, 14-17 and 67 depend from claim 3 and are also statutory. Claim 61 recites a physical transformation of matter (producing a library of proteins). It is noted that applicants specifically stated on page 15 of the response filed 11/26/04 that "producing" is intended to be a physical step of producing actual proteins.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

### ***Conclusion***

Claims 1, 2, 4, 18, 38-43, 45-50, 60, and 68 are rejected. All rejections and objections not reiterated above are hereby withdrawn. Claims 3, 5-7, 14-17, 44, 61 and 67 are allowed.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Monday-Friday; 6 am-2:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marjorie A. Moran  
Primary Examiner  
Art Unit 1631

*Marjorie A. Moran*  
12/10/05